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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WALICKA, MALGORZATA A	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/555,093	NAPIER, JOHNATHAN A.	
	Examiner	Art Unit	
	Malgorzata A. Walicka	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,12-14 and 39-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *39-43* is/are allowed.

6)☐ Claim(s) *1-7,12-14 and 44- 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: copy of prior art and sequence alignment used in rejection under 35 UDC, section 102.

The Amendment and Response filed on Nov. 10, 2003 is acknowledged. The amendments have been entered as requested. Claims 1, 13 and 42 are amended; claims 8-11 and 23 are cancelled; new claims 44-46 are added. Claims 1-7, 12-14 and 39-46 are pending and are the subject of this Office Action.

Detailed Office Action

1. Objections

Objection to claim 8 is moot because the claim has been canceled.

In the amended claim 1 the colon in the second line should be deleted.

2. Rejections

2.1. 35 U.S.C. section 101

Rejection of claims 1-14 and 23 made in the previous Office Action paper No.14 is withdrawn, because claim 1 has been amended.

2.2. 35 U.S.C. section 112, second paragraph

Rejection of claim 14 and 42 under 35 U.S.C. 112, second paragraph made in the previous Office Action is withdrawn, because the claims have been amended.

Rejection of claim 23 is moot because the claim has been cancelled.

2.3. 35 U.S.C. section 112, first paragraph

2.3.1. Lack of written description

Rejection of claims 8-11 and 23 is moot because the claims have been cancelled.

Amended claims 1-7, 12-14 and 46 are rejected under 35 U.S.C. 112, first paragraph, for the reasons stated in the previous Office Action and reiterated herein.

The claims are directed to a polypeptide having desaturase activity, which comprises one or more amino acid deletions, insertions or substitutions relative to a polypeptide comprising SEQ ID NO: 2, but has at least 90% amino acid sequence identity therewith.

Claims 1-7, 12, 14, 44 and 45 are directed to any polypeptide which has at least one addition, deletion, substitution and is at least 90% identical to another polypeptide comprising SEQ ID NO: 2 and wherein said claimed polypeptide has desaturase activity. Claims 1-7, 12, 14, 44 and 45 are rejected under this section of 35 USC 112, because the claims are directed to a genus of polypeptide comprising SEQ ID NO: 2 that comprise one or more amino acid deletions, insertions or substitutions of said polypeptide comprising SEQ ID NO: 2 and having any desaturase activity. Applicants, however, do not describe the claimed genus sufficiently, because the specificity of the claimed desaturase is not stated. The term desaturase does not describe a specific enzymatic activity; it encompasses a genus of enzymes, for example, desaturases Δ^4, Δ^6, Δ^{12}. Applicants disclose desaturase Δ^6 of SEQ ID NO:2, but no description has been provided of the common functional features of all polypeptides encompassed by the genus of the claims. No

information, beyond the characterization of SEQ ID NO:2 has been provided by applicants which would indicate that they had possession of the claimed genus of polypeptides. The specification does not contain any disclosure of the function of all desaturases within the scope of the claimed genus. As such, the claimed genus is diverse in functional features. Because the claimed genus is diverse in function, the single species SEQ ID NO:2 is not a representative of all members of the entire genus of desaturases, and is not sufficient to provide the identifying functional characteristics of the other members of the genus. The disclosure is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus.

In summary, the claimed polypeptides are insufficiently described in the disclosure, and one skilled in the art cannot reasonably conclude that the Applicants had possession of the claimed invention at the time the instant application was filed.

In addition, claim 2 is directed to a polypeptide of clam 1, wherein said polypeptide has a cytochrome domain. The claim is directed to a large and variable genus of polypeptides comprising any domain of any cytochrome from any organism or man- made, whereas the specification teaches only one representative of the genus, i.e. SEQ ID NO: 2 comprising the domain of cytochrome b_5, said domain having the structure underlined in Fig. 2 b, which is a species of the structure disclosed on page 5,

line 13-14. The specification fails to present any identifying characteristics of any domain of any cytochrome other than the described domain of cytochrome 5, which occupies a definite position in the protein of SEQ ID NO:2. Therefore, one skilled in the relevant art in not convinced that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Traversing the rejection of claim 2 Applicants write:

> "The specification describes the polypeptides of claim 2 as including functional (electron transport activity) and chemical (a heme group) properties. As evidenced by attached references [exhibits A-C], cytochrome domains were known in the art to the November 24, 1997 effective filing date of the application" (page 7, line 11).

Applicant's argument has been fully considered but is found not persuasive. The fact that cytochrome domains were known in the art to the November 24,1997 does not mean that Applicant used them to make their invention. Applicants do not disclose other construct than that containing domain of cytochrome 5 having the sequence identified in this application as SEQ ID NO: 3, i.e., Applicant disclose only one species of the claimed genus, which occupies a definite position in SEQ ID NO:2. The fact that one skilled in the art is enabled to make the invention, as claimed in claim 2 does not mean that Applicants disclosed said invention.

Furthermore, claim 5 is rejected because applicants fail to disclose any desaturase of claim 1 having at least three histidine boxes. Applicants invention, the desaturase of SEQ ID NO: 2, has only two histidine boxes as marked in Fig. 1.

Traversing this rejection Applicants argue, "The specification does disclose, however, the amino acid sequence of histidine boxes, 'H-X-X-H-H' and 'Q-X-X-H-H.' One of skill in the art could readily make and use a polypeptide having a third histidine box based on the disclosed amino acid sequence of SEQ ID NO: 2" (page 9, line 16 of Remarks).

Applicants' argument has been fully considered but is found not persuasive. Although one skilled in the art could modify the amino acid sequence of SEQ ID NO: 2 so that it contains the third histidine box, that does not mean that SEQ ID NO:2 modified to contain a third histidine box will retained the desired biological activity. The structure/function relationship as disclosed for SEQ ID NO;2 is not a representative of the structure/function relationship of the all members of the claimed genus of desaturases. For example, how can SEQ ID NO:2, which has only 2 histidine boxes be representative of a protein with three histidine boxes? The specification does not teach whether the position of the box matters; would proteins with boxes in different position be functionally different? If so, in what way? Does number of boxes matter? If so, how? Merely because one can make a variant does not mean Applicants have described it or that it is representative of all members of the claimed genus. The rejection is for lack of written description and not for enablement.

Furthermore, claim 46 is rejected as lacking structural and functional description. The claim is generic and the scope of the claim encompasses any desaturase

originating from a natural source or man made, because the part of SEQ ID NO: 2 can be even one amino acid. SEQ ID NO: 2, which set forth desaturase Δ^6 of *C. elegans*, is not a representative species of the genus of all desaturases. Without the structural and functional identification of the claimed invention one skilled in the art is not convinced that Applicant possessed the invention.

2.3.2. Scope of enablement

Rejection of claims 8-11 and 23 is moot because the claims have been cancelled.

Claims 1-7, 12, 14 and 44-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *C. elegans* Δ^6 desaturase set forth by SEQ ID NO: 2, does not reasonably provide enablement for any polypeptide having desaturase activity, which comprises one or more amino acid deletions, insertions or substitutions relative to a polypeptide comprising SEQ ID NO: 2, but has at least 90% amino acid sequence identity therewith or for the polypeptide having desaturase activity and comprising a part of amino acid sequence of SEQ ID NO:2.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claims are directed to any desaturase comprising a polypeptide comprising SEQ ID NO: 2, and variants of said polypeptides that are at least 90% identical to said polypeptide or to any desaturase comprising part of SEQ ID NO: 2. The scope of the claims is not commensurate with the enablement

provided by the disclosure with regard to the extremely large number of proteins and their properties broadly encompassed by the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)), otherwise undue experimentation is necessary.

Factors to be considered in determining whether undue experimentation is required to make the claimed invention are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses any desaturase from any natural source, or man-made, that comprises a polypeptide comprising the amino acids sequence of SEQ ID NO: 2 and having at least 90% identity to the polypeptide comprising SEQ ID NO: 2 or any desaturase that comprises part of SEQ ID NO: 2 .

Although the methods of gene cloning and modification are well developed and skills of artisans are high, it is not a routine in the art to clone all possible desaturases from all natural or man made sources and select those that are at least 90 % identical to a polypeptide comprising SEQ ID NO: 2. Also, it is not a routine experimentation in the art to modify SEQ ID NO: 2 by making deletions, insertions and substitutions and addition of any flanking amino acids so that resulting protein were in at least 90%

identical to any other polypeptide containing SEQ ID NO: 2. Probability of success in making the invention is very low absent of teachings regarding the structure of said polypeptide comprising SEQ ID NO: 2. Also, it is not a routine in the art (claim 46) to screen any protein comprsing a part, i.e. even on or two amino acids, from any natural and man-made sources for enzymatic activity of all possible desaturases.

The specification does not support the broad scope of the claims. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed so that the claimed species of desaturases could be obtained. The provision of SEQ ID NO: 2 fails to provide such guidance of polypeptides that comprise SEQ ID NO: 2 and are all at least 90% identical to each other. The provision of SEQ ID NO: 2 does not provide guidance for structure and specific function of all possible desaturases as claimed. One skilled in the art would have no expectation of being able to create variants of SEQ ID NO: 2 with other desaturases activities (for example Δ^{12} desaturase) without undue experimentation, but such proteins are encompassed by the claims.

In conclusion, one skilled in the art would require additional guidance, regarding the structure and function of the claimed invention. Without such guidance, the experimentation left to those skilled in the art is undue.

In their Remarks Applicants state, page 13, line 17, "The specification discloses examples of amino acid residues that can be substituted for other amino acid residues 'without eliminating a desired property of that polypeptide (such as desaturase activity).' Page 7, lines 19-20. See page 7, line 21 to page 8, line 2 for examples of amino acid substitutions."

The quoted passage of the specification refers to the so-called "conservative" or "semi-conservative" substitutions of one amino acid by another. However, Applicants do not teach which particular residues of SEQ ID NO: 2 may be conservatively substituted without the change in function of desaturase Δ^6 of that protein, because the structure to function relationship is not disclosed for SEQ ID NO: 2. Furthermore, Applicants' claims are directed to any desaturase the specific function and function/structure relationships are not enabled in the specification. In summary, the polypeptide having any desaturase activity whose structure comprises a polypeptide being at least 90% identical to SEQ ID NO: 2 are not enabled. The disclosure is also not enabling for any desaturase comprising any part of SEQ ID NO: 2.

2.4. 35 U.S.C., section 102

Amended claim 13 and new claim 46 are rejected under this section.

Claim 13 is directed to an isolated and purified polypeptide consisting of part of SEQ ID NO: 2. A part of SEQ ID NO: 2 consisting of amino acid methionine which

occupies position 1 in SEQ ID NO: 2 is disclosed in the Aldrich catalog, Aldrich Chemical Company, Inc. 1990, page 830; see the attached copy.

Claim 46 is directed to an isolated and purified polypeptide having desaturse activity, which comprises a part of the amino acid sequence as shown in SEQ ID NO: 2.

US Patent 5,614,393, filed Dec. 30, 1994, discloses Δ^6 desaturase that has in positions 274-381 the same amino acids as those in positions 383-390 of SEQ ID NO: 2 of the instant application; see the enclosed alignment.

3. Conclusion

Claims 39-43 are allowed. The reasons for allowable subject matter were stated in the Office Action of August 13, 2002.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (571) 272-0944 and the right fax number is (571) 273-0944. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m. EST.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (571) 272-0928. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to

Malgorzata A. Walicka, Ph.D.

Patent Examiner

Art Unit 1652

REBECCA E. PROUTY
PRIMARY EXAMINER
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